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(54) Title: COMPOSITIONS FOR THE TREATMENT OF CHRONIC INFECTIONS CONTAINING GLUCOCORTICOID AND ANTI-GLUCOCORTICOID

(57) Abstract

A glucocorticoid, such as cortisol or a derivative or analogue thereof, and an anti-glucocorticoid, such as dehydroepiandrosterone (DHEA) or a derivative or analogue thereof, are used simultaneously, separately or sequentially in treatment of chronic infections such as tuberculosis, HIV infection, leishmaniasis and syphilis.

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A. CLASSI	FICATION OF SUBJECT MATTER	1	
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	ENTS CONSIDERED TO BE RELEVANT	wont nassanas	Relevant to claim No.
Category °	Citation of document, with indication, where appropriate, of the rele	Valit Passanges	
х	US 5 387 583 A (LORIA ROGER M) 7	February	1-19
^	1995	l est dat y	* *-
	see abstract		
	see page 4, line 20-29		
	see page 5, line 45-68; examples	1-6	
х	WO 91 04030 A (UNIV UTAH) 4 Apri	1 1991	1-5,8-12
	see page 13, line 25 - page 14,		-
	figures 2A,2B,2C; example 2		
	see claim 4; example 4		
P,X	US 5 540 919 A (DAYNES RAYMOND A	ET AL)	1-5,
,,,,	30 July 1996		8-12,
	5 11 - 51 54 - 1-i 0	10.	14-18
	see page 5, line 51-64; claims 9- figures 2A,2B,2C,4	-12;	
	11gures 2A,2B,2C,4		
		-/	
X Furth	ner documents are listed in the continuation of box C.	X Patent family members are listed in	n annex.
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	Tel. (+31-70) 340-2040, Tx. 31 651 epo ni,	Gonzalez Ramon, N	

In Itional Application No PCT/GB 97/01653

		PC1/GB 9//01653		
	ation) DOCUMENTS CONSIDERED TO BE RELEVANT			
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.		
A	US 5 077 284 A (LORIA ROGER M ET AL) 31 December 1991 see abstract see page 11, line 35-45 see page 13, line 55-68; claims 1-3	1-19		
A	WISNIEWSKI TL ET AL: "The relationship of serum DHEA-S and cortisol levels to measures of immune function in human immunodeficiency virus-related illness." AM J MED SCI, FEB 1993, 305 (2) P79-83, UNITED STATES, XP002044510 see page 80, column 1, paragraph 1; figure 3	1,2,4-6, 8,9, 11-15		
A	BAKER R.W. ET AL: "Tuberculosis, steroid metabolism and immunity" QJM - MONTHLY JOURNAL OF THE ASSOCIATION OF PHYSICIANS, 1996, 89/5 (387-394), UNITED KINGDOM, XP002044502 see page 388, column 2, paragraph 2 - page 389, column 1, paragraph 2 see page 390, column 2, paragraph 4	1,2,4-6, 8,9, 11-15		
A	ROOK G A W ET AL: "Pathogenetic role, in human and murine tuberculosis, of changes in the peripheral metabolism of glucocorticoids and antiglucocorticoids" PSYCHONEUROENDOCRINOLOGY, 22 (SUPPL. 1). 1997. S109-S113., XP002044516 see page 112, paragraph 3	1-19		
A	DE 38 12 595 A (COLTHURST LTD ;PRENDERGAST PATRICK THOMAS (IE)) 27 October 1988 see abstract; claims 3-6; examples 8,9	1-19		
A	WO 95 30418 A (UNIV JOHNS HOPKINS) 16 November 1995 see abstract see page 3, line 19-30; claims 1,9,11,13	1-19		

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. .ernational application No. PCT/GB 97/01653

INTERNATIONAL SEARCH REPORT

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)
This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:
1. X Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely: see FURTHER INFORMATION sheet PCT/ISA/210
Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful international Search can be carried out, specifically: see FURTHER INFORMATION sheet PCT/ISA/210
Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).
Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)
This International Searching Authority found multiple inventions in this international application, as follows:
As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
Remark on Protest The additional search fees were accompanied by the applicant's protest. No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

Claims Nos.: 1-13

because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

In view of the large number of compounds, which are defined by the general definition in the independent claims, the search had to be restricted for economic reasons. The search was limited to the compounds for which pharmacological data was given and/or the compounds mentioned in the claims, and to the general idea underlying the application (see Guidelines, Part B, Chapter III, paragraph 3.6).

Remark: Although claims 14-19 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

Information on patent family members

tr. ational Application No
PCT/GB 97/01653

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 5387583 A	07-02-95	WO 9423722 A	27-10-94
WO 9104030 A	04-04-91	AU 652130 B AU 6501990 A AU 667018 B AU 7572794 A CA 2066716 A EP 0494224 A JP 2505313 B JP 5502856 T US 5540919 A US 5562910 A US 5518725 A	18-08-94 18-04-91 29-02-96 08-12-94 26-03-91 15-07-92 05-06-96 20-05-93 30-07-96 08-10-96 21-05-96
US 5540919 A	30-07-96	AU 652130 B AU 6501990 A AU 667018 B AU 7572794 A CA 2066716 A EP 0494224 A JP 2505313 B JP 5502856 T WO 9104030 A US 5562910 A US 5518725 A	18-08-94 18-04-91 29-02-96 08-12-94 26-03-91 15-07-92 05-06-96 20-05-93 04-04-91 08-10-96 21-05-96
US 5077284 A	31-12-91	US 5461042 A US 5407684 A	24-10-95 18-04-95
DE 3812595 A	27-10-88	AT 401470 B AT 98488 A AU 608824 B AU 1467888 A BE 1004315 A CA 1325594 A CH 675358 A DK 208188 A FR 2615394 A GB 2204237 A,B GR 88100248 A	25-09-96 15-02-96 18-04-91 20-10-88 03-11-92 28-12-93 28-09-90 17-10-88 25-11-88 09-11-88 31-01-89

Information on patent family members

In alional Application No
PCT/GB 97/01653

Patent document cited in search report	Publication date		Patent family member(s)	Publication date
DE 3812595 A		JP	1025722 A	27-01-89
		JP	2577771 B	05-02-97
		KR	9614988 B	23-10-96
		LU	87202 A	17-11-88
		NL	8800926 A	16-11-88
		NZ	236303 A	27-07-97
		OA	8729 A	31-03-89
		PH	25907 A	19-12-91
		SE	503482 C	24-06-96
		SE	8801406 A	17-10-88
		US	4956355 A	11-09-90
WO 9530418 A	16-11-95	AU	2473695 A	29-11-95